

DOCKET NO.: IBIS-0261



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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PATENT

In Re Application of:  
Griffey et al.

Serial No.: 09/499,875

Group Art Unit: 1627

Filing Date: February 8, 2000

Examiner: T. Prasthofer

For: OPTIMIZATION OF LIGAND AFFINITY FOR RNA TARGETS USING MASS  
SPECTROMETRY

DATE OF DEPOSIT: 7/3/01

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FOR PATENTS, WASHINGTON, DC 20231.

Mitchell R. Brustein  
Mitchell R. Brustein  
REGISTRATION NO.: 38,394

Box ☐ NON-FEE  
☐ AF

Assistant Commissioner for Patents  
Washington DC 20231

Sir:

### AMENDMENT TRANSMITTAL LETTER

Transmitted herewith for filing in the above-identified patent application is:

- ☐ A Preliminary Amendment.
- ☒ An Reply Responsive to the Office Action Dated April 10, 2001.
- ☐ An Amendment Supplemental to the Paper filed \_\_\_\_\_.
- ☐ Other: \_\_\_\_\_.

- ☒ Applicant(s) has previously claimed small entity status under 37 CFR §1.27.
- ☐ Applicant(s) by its/their undersigned attorney, claims small entity status under 37 CFR §1.27 as:
- ☐ an Independent Inventor
  - ☐ a Small Business Concern
  - ☐ a Nonprofit Organization
- ☐ This application is no longer entitled to small entity status. It is requested that this be noted in the files of the Patent and Trademark Office.
- ☐ Substitute Pages \_\_\_\_\_ of the Specification are enclosed.
- ☐ An Abstract is enclosed.
- ☐ \_\_\_\_\_ Sheets of Proposed Corrected Drawings are enclosed.
- ☐ A Certified Copy of each of the following applications: \_\_\_\_\_  
\_\_\_\_\_ is enclosed.
- ☐ An Associate Power of Attorney is enclosed.
- ☐ Information Disclosure Statement.
- ☐ Attached Form 1449.
  - ☐ A copy of each reference as listed on the attached Form PTO-1449 is enclosed herewith.
- ☐ Appended Material as follows: \_\_\_\_\_
- ☐ Other Material as follows: \_\_\_\_\_

## FEE CALCULATION

☐ No Additional Fee is Due.

				SMALL ENTITY		NOT SMALL ENTITY	
	REMAINING AFTER AMENDMENT	HIGHEST PAID FOR	EXTRA	RATE	FEE	RATE	FEE
TOTAL CLAIMS	120	120 (20 MINIMUM)	0	\$9 EACH	\$ 0	\$18 EACH	\$
INDEP. CLAIMS	12	12 (3 MINIMUM)	0	\$40 EACH	\$0	\$80 EACH	\$
FIRST PRESENTATION OF MULTIPLE DEPENDENT				\$135	\$	\$270	\$
<input type="checkbox"/> ONE MONTH EXTENSION OF TIME				\$55	\$	\$110	\$
<input checked="" type="checkbox"/> TWO MONTH EXTENSION OF TIME				\$195	\$ 195	\$390	\$
<input type="checkbox"/> THREE MONTH EXTENSION OF TIME				\$445	\$	\$890	\$
<input type="checkbox"/> FOUR MONTH EXTENSION OF TIME				\$695	\$	\$1390	\$
<input type="checkbox"/> FIVE MONTH EXTENSION OF TIME				\$945	\$	\$1890	\$
<input type="checkbox"/> LESS ANY EXTENSION FEE ALREADY PAID				minus	(\$ )	minus	(\$ )
<input type="checkbox"/> TERMINAL DISCLAIMER				\$55	\$	\$110	\$
<input type="checkbox"/> OTHER FEE OR SURCHARGE AS FOLLOWS:							
TOTAL FEE DUE					195		\$

- ☒ A Check is Enclosed in the Foregoing Amount Due.
- ☒ Petition is hereby made under 37 C.F.R. 1.136(a) to extend the time for response to the Office Action of **April 10, 2001** to and through **July 10, 2001** comprising an extension of the shortened statutory period of **2 month(s)**.
- ☒ The Commissioner is hereby requested to grant an extension of time for the appropriate length of time, should one be necessary, in connection with this filing or any future filing submitted to the U.S. Patent and Trademark Office in the above-identified application during the pendency of this application. The Commissioner is

further authorized to charge any fees related to any such extension of time to deposit account 23-3050. This sheet is provided in duplicate.

- ☒ The Commissioner is authorized to charge payment of the following fees and to refund any overpayment associated with this communication or during the pendency of this application to deposit account 23-3050. This sheet is provided in duplicate.
- ☐ The Foregoing Amount Due for Filing this Paper.
- ☒ Any additional filing fees required, including fees for the presentation of extra claims under 37 C.F.R. 1.16.
- ☒ Any additional patent application processing fees under 37 C.F.R. 1.17 or 1.20(d).

**SHOULD ANY DEFICIENCIES APPEAR** with respect to this application, including deficiencies in payment of fees, missing parts of the application or otherwise, the United States Patent and Trademark Office is respectfully requested to promptly notify the undersigned.

Date: 7/3/01



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For: OPTIMIZATION OF LIGAND AFFINITY FOR RNA TARGETS USING  
MASS SPECTROMETRY

I, Mitchell R. Brustein, Registration No. 38,394 certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

On

7/3/01

  
\_\_\_\_\_  
Mitchell R. Brustein, Registration No. 38,394

Assistant Commissioner  
for Patents  
Washington, D.C. 20231

**REPLY UNDER 37 C.F.R. §§ 1.142 AND 1.146**  
**TO OFFICE ACTION DATED April 10, 2001**

A restriction has been required to one of 13 groups of inventions said to be defined by the claims. Applicants respectfully request that this restriction be reconsidered, and that the number of inventive groups be reduced to take account of apparent interrelationships among the claimed inventions.

The pending claims have been classified as Groups I-XIII. Group I (Claims 1-29) is allegedly drawn to a method for selecting ligands that have an affinity for a target molecule. Group II (Claims 30-46) is allegedly drawn to a method for selecting members of a group of compounds that can form a non-covalent complex with a target molecule and where the affinity of the members for the target molecule is greater than a baseline affinity. Group III (Claims 47-

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52) is allegedly drawn to a method of detecting small molecule-RNA complexes having an affinity expressed as a dissociation constant of from about nanomolar to about 100 millimolar. Group IV (Claims 53-56) is allegedly drawn to a method of detecting small molecule-RNA complexes having from about nanomolar to about 100 millimolar affinity as measured as a dissociation constant. Group V (Claims 57-60, 63, 65, and 120) is allegedly drawn to a method for determining the relative interaction between at least two ligands with respect to a target substrate. Group VI (Claims 61 and 62) is allegedly drawn to a method of determining binding interaction between a first ligand and a second ligand. Group VII (Claim 64) is allegedly drawn to a method of determining the relative proximity of binding sites for a first ligand and a second ligand on a target substrate. Group VIII (Claims 66-68) is allegedly drawn to a method of determining the relative orientation of a first ligand to a second ligand when bound to a target substrate. Group IX (Claims 69-78) is allegedly drawn to a screening method for determining compounds having binding affinity to a target substrate. Group X (Claims 79-114) is allegedly drawn to a method for modulating the binding affinity of ligands for a target molecule. Group XI (Claims 115-118) is allegedly drawn to a method for refining the binding of a ligand to a target molecule. Group XII (Claim 119) is allegedly drawn to a compound. Group XIII (Claims 94, 95, and 96) is allegedly drawn to a method of refining binding by virtually concatenating ligand fragments to form a 3D model. The Examiner has further required an election of species. Applicant respectfully traverses this restriction requirement as the subject matter of each of the groups is not divergent, and would not pose a burden to search simultaneously.

The claims of a patent application may be restricted if two or more inventions are, *inter alia*, independent. 35 U.S.C. §121. The purpose of § 121 is to avoid a situation that requires separate and diverse searches to be conducted on claims directed to independent (unrelated) subject matter. Inventions are deemed "independent" if there is no disclosed relationship and/or if the inventions are unconnected in design, operation or effect. *See* M.P.E.P. §802.01.

Although the Office Action contends that Groups I, II, III, and IV encompass different methods of use which are "driven by different objectives, entail different reagents and result in

different products," Groups I, II, III, and IV do *not* entail different reagents or result in different products. In particular, each of these groups involve selecting chemical moieties having affinity for a target molecule. In Group I, the chemical moieties are ligands. In Group II, the chemical moieties are members of a group of compounds. In Groups III and IV, the chemical moieties are small molecules and the target molecule is RNA. As such, the subject matter of Groups I, II, III, and IV is not divergent and would not pose a burden to search simultaneously.

Reclassification is also warranted for Groups V-VIII. Although the Office Action contends that these groups encompass different methods of use which are "driven by different objectives, entail different reagents and result in different products," each group relates to methods for determining the interaction between two ligands. In Group V, a relative interaction between two ligands is determined with respect to a target substrate. In Group VI, the relative interaction is a binding interaction. In Group VII, the relative interaction is a relative proximity. In Group VIII, the relative interaction is a relative orientation. As such, the subject matter of Groups V, VI, VII, and VIII is not divergent and would not pose a burden to search simultaneously.

There similarly is insufficient basis for the Office Actions' suggestion that Group IX is divergent from Groups X and XI. Each of these groups relate to effectuating a concatenation between two ligands. In Group IX, ligands that bind to a target non-competitively are identified and concatenated to form a third ligand. In Group X, the ligands are ligand fragments. In Group XI, the ligand fragments are virtual ligand fragments. As such, the subject matter of Groups IX, X, and XI is not divergent and would not pose a burden to search simultaneously.

The proposed restriction among Groups X and XI also lacks adequate basis. Although the Office Action contends that Groups X and XI encompass processes which are "borne of different objectives, utilize different reagents, and result in different products," as discussed above, Groups X and XI both relate to effectuating a concatenation between two ligands. Accordingly, the subject matter of those groups is not divergent and would not pose a burden to search simultaneously.

Alignment of Group XII with Groups IX, X, and XI is also warranted. Although Group XII relates to products while Groups IX, X, and XI relate to processes for making or using the product, even the Office Action acknowledges that the products will be examined along with the invention encompassed by Groups IX, X, and XI (*see* Office Action at paragraph 9). Since Group XII encompasses products, Group XII is properly included in Groups IX, X, and XI.

Lastly, Applicants note that the Office Action included Claims 94-96 within both Group X and Group XIII. However, Group XIII (like Groups IX, X, and XI) relates to effectuating a concatenation between two ligands. Accordingly, the subject matter of Group XIII is not divergent from that of Groups IX, X, and XI.

Accordingly, Applicants respectfully request that the pending claims be restricted, if at all, into three groups, as follows:

Group I: Claims 1-56

Group II: Claims 57-68 and 120

Group III: Claims 69-119

Nevertheless, in accordance with 37 C.F.R. § 1.143, Applicants hereby provisionally elect the claims of Group II (Claims 30-46) for prosecution. The Examiner has further required an election of species. Applicant hereby elects the species wherein the collection library of diverse compounds comprises a collection of drug substances and the target molecule is RNA. Claims 30-46 read on the elected species.

Further, in the event that the Examiner amends the restriction requirement as proposed to incorporate Groups I-IV into a single group, Applicant also hereby elects the species wherein the standard ligand is ammonium and the mass spectrometer includes Z-spray mass spectrometers including mass analysis by quadrupole detectors. Claims 1-7 and 9-56 read on the elected species.

It is Applicant's understanding that the above election is being made to aid the Examiner

in conducting a search and examination of the claimed subject matter, and is not to be construed as limiting the scope of Applicant's claims. It is also Applicant's understanding that, if the elected subject matter is found to be allowable over the prior art, the search and examination will be expanded to cover other species, until it includes the full scope of the generic claims included in the elected group.

Applicants hereby affirm the right to file one or more divisional applications with respect to any of the non-elected subject matter.

Applicants believe that the foregoing constitutes a complete and full response to the Office Action of record. Accordingly, an early and favorable action on the merits is requested respectfully.

Respectfully submitted,



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Date: 7/3/01

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